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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/734,644	12/15/2003	Jay Bua	029488-0112	9030

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EXAMINER	
FETTEROLF, BRANDON J	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 02/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/734,644	BUA, JAY	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 November 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *13-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Bua, Jay

Response to the Amendment

The Amendment filed on 11/21/2005 in response to the previous Non-Final Office Action (08/23/2005) is acknowledged and has been entered.

Claims 1-22 are currently pending.

New claims 13-22 are withdrawn from consideration as being drawn to subject matter which would require a new search and different considerations for patentability.

Claims 1-12 are currently under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

All rejections and/or objections are withdrawn in view of applicant's amendments.

New Rejections necessitated by the amendment:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-10 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mauvais-Jarvis (US 4,919,937, 1990, IDS) as evidenced by Mauvais-Jarvis (Cancer Research 1986; 46: 1521-1525) in view of Atkinson et al. (Cancer Epidemiology, Biomarkers & Prevention 1999; 8: 863-866, IDS) as evidenced by Boyd et al. (J. Nat. Cancer Inst. 1995; 87: 670-675) and Kolb et al. (Radiology 2002; 225; 165-175).

Mauvaris-Jarvis et al. teach (column 4, lines 46-53) a method of treating conditions of the breast comprising administering percutaneously an aqueous alcoholic gel comprising trans-4-hydroxy tamoxifen, wherein the aqueous alcoholic gel enables percutaneous penetration to take place and comprises Carbopol ®, ethyl alcohol/water and 0.15g of 4-hydroxy tamoxifen (column 3, lines 29-39). With regards to the conditions of the breast, the patent teaches (column 4, lines 37-39) that the breast conditions include, but are not limited to, benign and cancerous conditions of the breast. Moreover, Mauvaris-Jarvis et al. teach that percutaneous administration of 4-hyrdroxytamoxifen overcomes the harmful side effects associated with oral administration of 1- to 30 mg/day of tamoxifen such as paradoxical stimulation of the ovaries by passing through the cutaneous barrier and being taken up directly by the receptors molecules in the tumors. Thus, while Mauvaris-Jarvis et al. do not specifically teach that the 4-hyroxy tamoxifen is administered as a racemic mixture of both trans and cis isomer, the claimed limitation would be an inherent property of the percutaneous administration of trans-4-hydroxy tamoxifen because as evidenced by Mauvais-Jarvis (Cancer Research 1986; 46: 1521-1525, IDS), percutaneous administration of the trans-4-OHTAM resulted in an equal yield of the cis and trans isomers of 4-OHTAM from breast tissue (page 1522, 2nd column, 6th paragraph). Thus, it does not appear that the claimed limitation results in a manipulative difference in the products used when compared to the prior arts disclosure. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int.

Mauvaris-Jarvis et al. do not explicitly teach that percutaneous administration of 4-hydroxy tamoxifen reduces dense breast tissue in a patient having class III or class IV dense breast tissue.

Atkinson et al teach the effects of tamoxifen on mammographic density, wherein mammograms from 94 women who had received tamoxifen for breast cancer and 188 women (without breast cancer) who had not received tamoxifen were visually classified according to the Wolfe pattern (abstract). Specifically, the reference teaches (page 865, Table 2 and page 864, 1st column, *Data Analysis*) administration of tamoxifen to patients having N1, P1, P2 or DY breast

density Wolfe pattern, wherein N1 represents the most lucent pattern and DY represents the most dense pattern. The reference further teaches (page 865, Table 2 and 2nd column, last paragraph) that tamoxifen treatment resulted in a reduction in mammographic breast density. As such, Atkinson et al. conclude (page 866, 1st column, last paragraph) that an additional benefit of reducing breast density by tamoxifen treatment may relate to the effectiveness of mammographic breast screening, wherein the reduction in breast density may provide benefits in terms of diagnosis at an earlier physiological stage and, thus, improved survival rates from breast cancer. Thus, while Atkinson et al. does not explicitly teach that the breast tissues are class III and/or class IV dense breast tissue, a patient having a the most dense DY breast pattern and/ or a P2 pattern on the Wolfe scale would meet the limitation of a Class III or Class IV dense breast composition because as evidenced by Kolb et al., the American College of Radiology has developed a classification system for breast composition, wherein class 3 is breast tissue heterogeneously dense and class 4 is highly dense (page 166, 3rd column, 1st paragraph). Hence, it does not appear that the claimed limitation and/or category result in a manipulative difference between the prior arts disclosure. Moreover, although Atkinson et al. does not explicitly teach that the breast tissues having a DY pattern includes dense tissue that is diffuse or nodular, the claimed limitation would be an inherent property of breast tissue characterized as DY because as evidenced by Boyd et al., DY describes a breast in which the parenchyma is occupied by both diffuse or nodular densities (page 670, 2nd column, 2nd paragraph). Thus, it does not appear that the claimed limitation results in a manipulative difference in the products used when compared to the prior arts disclosure. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to administer 4-hydroxy tamoxifen percutaneously to a patient suffering from class III or class IV dense breast tissue as taught by Mauvaris-Jarvis et al. in view of Atkinson et al.. One would have been motivated to do so because as taught by Atkinson et al, tamoxifen treatment

results in the reduction in breast density which may lead to better diagnosis of breast cancer by mammographic techniques. Thus, one of ordinary skill in the art would have a reasonable expectation of success that by administering 4-hydroxy tamoxifen percutaneously to a patient having class III or class IV dense breast tissue, one would achieve method of reducing breast density and increasing the sensitivity of mammograms for detecting breast cancer.

Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Mauvais-Jarvis et al. (US 4,919,937, 1990, IDS) as evidenced by Mauvais-Jarvis (Cancer Research 1986; 46: 1521-1525) and Atkinson et al. (Cancer Epidemiology, Biomarkers & Prevention 1999; 8: 863-866, IDS) as evidenced by Boyd et al. (J. Nat. Cancer Inst. 1995; 87: 670-675) Kolb et al. (Radiology 2002; 225; 165-175) in view of Tan et al. (AAPS PharmSciTech 2000; 1; Article 24) and Alberti et al. (Journal of Controlled Release 2001; 71: 319-327).

Mauvais-Jarvis et al. and Atkinson et al. teach, as applied to claims 1-10 and 12 above, a method of reducing breast density, comprising administering 4-hydroxy tamoxifen percutaneously to a patient having a class III or class IV dense breast composition. Specifically, Mauvais-Jarvis et al. teach that the formulation comprises an aqueous alcoholic gel comprising trans-4-hydroxy tamoxifen, wherein the aqueous alcoholic gel enables percutaneous penetration to take place and comprises Carbopol ®, ethyl alcohol/water and 0.15g of 4-hydroxy tamoxifen (column 3, lines 29-39).

Mauvais-Jarvis et al. and Atikinson et al. do not explicitly teach that the hydroalcoholic gel comprises ethyl alcohol, isopropyl myristate, and hydroxypropylcellulose.

Tan et al. teach (2nd page, 1st column, 1st full paragraph) that hydrophilic polymers have been used mainly to improve the bioadhesive properties of buccal preparations, wherein the hydrophilic polymers include but are not limited to Carbopol and hydroxypropyl cellulose.

Alberti et al. teach (Title) the in vivo assessment of enhanced topical delivery of terbinafine to human stratum corneum. Specifically, the reference teaches that the formulation was based on a vehicle consisting of ethanol and isopropyl myristate (abstract).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substitute a hydroalcoholic gel comprising ethanol, water and Carbopol for a hydroalcoholic gel comprising ethyl alcohol, isopropyl myristate and hydroxypropylcellulose. One

would have been motivated to do so because each has been taught in the prior art as being equivalents suitable for the same purpose. As such, one of ordinary skill in the art would have a reasonable expectation of success that by substituting a hydroalcoholic gel comprising ethanol, water and Carbopol for a hydroalcoholic gel comprising ethyl alcohol, isopropyl myristate and hydroxypropylcellulose, one would achieve an effective formulation for percutaneous administration.

Therefore, NO claim is allowed

All other rejections and/or objections are withdrawn in view of applicant's amendments and arguments there to.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 8:30 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Brandon J Fetterolf, PhD
Examiner
Art Unit 1642

BF

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER
2/16/06